REMARKS

Reconsideration of this Application is respectfully requested.

Status of the claims

Claims 39, 56,and 88-90 are canceled herein without prejudice or disclaimer. Claims 1, 28, 41, 51, 61, 69, and 77 are amended herein. Upon entry of this amendment, claims 1, 2-4, 6-26, 28, 30-34, 36, 37, 41, 43-55, 57, 60-87, and 91-96 will be pending in the application. Claims 2-4, 6-15, 18-26, 31-34, 36, 37, 43-50, 63-68, 71-76, and 79-84 have been withdrawn from consideration. Applicants note that the Office Action of October 20, 2006 designated claim 62 as withdrawn on page 2, and believe this was an inadvertent error, as claim 62 contains the same subject matter as previously presented claims 70 and 78 that are not withdrawn from consideration as a result of the election of species by Applicant of August 2, 2006, and claim 62 was also included in the rejection under U.S.C. 103 (a) on page 7 of the Office Action. Applicants therefore designate and consider claim 62 herein as "previously presented". Claims 1, 16, 17, 28, 30, 41, 51-55, 57, 60-62, 69, 70, 77, 78, 85-87, and 91-96 are therefore under prosecution upon entry of the present amendment.

Claim Amendments

Applicants have canceled claims 39, 56, and 88-90 herein without prejudice or disclaimer, expressly reserving the right to prosecute these claims, or claims based on the subject matter of these claims, in other applications, such as continuation applications.

Applicants have herein amended claims 1, 28, 41, and 51 to expedite prosecution of the application. Amended independent claims 1, 41, and 51 now recite in vitro synthesis systems, kits, and compositions comprising an extract of E. coli cell that does not express Gam and that has reduced activity of a nuclease as a result of mutation, in which the extract has been modified by the addition of Gam protein. Support for this amendment can be found throughout the specification as filed. For example, extracts of E. coli cells modified by the addition of an inhibitor such as Gam protein are found at least in paragraphs [0038] and [0093], and the addition of Gam protein to a cell lysate is disclosed, for example, in Examples 6 and 7. Claim 28 has been amended so that its language conforms to that of amended claim 1, from which it depends. These amendments add no new matter, and their entry is respectfully requested.

Claims 61, 69, and 77 have been amended to correct a typographical error in which the claims included the phrase "wherein said nuclease in a DNase". The phrase has now been corrected by amendment to read "wherein said nuclease is a DNase". No new matter has been introduced by this correction. Entry of the amendments is therefore respectfully requested.

Claims Objections

Claims 61, 69, and 77 are objected to because of the phrase "said nuclease in", which should say instead "said nuclease is". Applicants have amended claims 61, 69 and 77 to recite "said nuclease is". Applicants therefore respectfully requested that the objection to claims 61, 69, and 77 be removed.

Claims Rejections under 35 U.S.C. §103(b), Pratt and Yu

Claims 1, 16, 17, 27, 28, 30, 35, 39, 41, 42, 51-60, 85, 88, 91, and 94 have been rejected as being obvious under 35 U.S.C. §103(a) over Pratt (*Coupled Transcription-Translation in Prokaryotic Cell-Free Systems*, Chapter 7 of Transcription and Translation: a Practical Approach Hanes, B.D., and Higgins, S.J., eds. (1984))in view of Yu et al (Proc. Natl. Acad. Sciences 97: 5978-5983 (2000)). Applicants note that claims 27, 35, 42, 58, and 59 were canceled in a previous response to Office Action. Claims 39, 56, and 88 are canceled herein, rendering their rejection moot. Applicants therefore herein address the rejection of claims 1, 16, 17, 28, 30, 41, 51-55, 57, 60, 85, 91, and 94.

Applicants respectfully disagree that claims 1, 16, 17, 28, 30, 41, 51-55, 57, 60, 85, 91, and 94 are rendered obvious by Pratt in combination with Yu et al. However, to expedite allowance of claims, and not in acquiescence to the rejection, applicants have amended independent claims 1, 41, and 51. Amended claims 1, 41, and 51 now recite an in vitro protein or nucleic acid synthesis system that comprises at least one extract from an E. coli cell that does not express Gam, in which the E. coli cell has a mutation that reduces the activity of at least one nuclease and in which the extract is modified by the addition of Gam protein. Applicants assert that a *prima facie* case for obviousness has not been made with respect to claims 1, 16, 17, 28, 30, 41, 51-55, 57, 60, 85, 91, and 94.

The MPEP states that to establish a *prima facie* case of obviousness there must be some suggestion or motivation in the prior art to make the claimed invention, there must be a reasonable expectation of success, and the prior art reference must teach or suggest all of the claim limitations. MPEP § 2142; In re Vaeck, 947 F.2d 488, 20 USPQ2d, 1438 (Fed. Cir. 1991). The reference teachings must be sufficient for one of ordinary skill in the relevant art having the

reference before him or her to make the proposed substitution, combination, or other modification. In re Linter, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972). MPEP 2143.01. Further, in making a rejection based on obviousness, the Examiner must consider the invention as a whole. Bausch & Lomb v. Barnes-Hind/Hydrocurve, Inc., 796 F.2d 443, 447-49, 230 USPQ 416, 419-20 (Fed. Cir. 1986), cert. denied, 484 U.S. 823 (1987). MPEP 2141.02. Applicants assert that the requirements of a rejection under 35 U.S.C. §103(b) are not been met for at least the following reasons.

First, the cited references do not disclose each and every claim limitation. Independent claims 1, 41, and 51 recite an in vitro synthesis system, a kit, and a composition that include an E. coli cell extract, in which the E. coli cell used to make the extract has a mutation that reduces the activity of a nuclease, in which the cell does not express Gam, and in which the extract is modified by the addition of Gam protein. Neither Pratt nor Yu et al. disclose Gam protein as recited in amended claims 1, 41, and 51.

Second, neither Pratt or Yu et al., alone or in combination, suggest or provide motivation for making of an *in vitro* synthesis system with a cell extract that includes added Gam protein. As argued in a previous response, Pratt, in discussing the use of linear DNA templates in E. coli *in vitro* synthesis systems, also does not anywhere suggest or provide motivation for the use of an inhibitor of recBC. Pratt in fact provides two alternative methods for preparing extracts having reduced reBC activity: the method of Zubay (pages 200-201) and the method of Gold and Schweiger (pages 201-202), both of which rely on the use of extracts of recB mutant cells and removal of DNA fragments from the extracts. Neither method includes the addition of a protein inhibitor of recB to a cell lysate used in the IVT system.

The Office Action of October 20, 2006 states that: "Yu et al. teach that one can alternatively inhibit the RecBCD exonuclease using the lambda phage Gam protein." Applicants do not agree that Yu et al. teach inhibition of a nuclease by addition of a protein, and particularly, as recited in the claims as amended, by addition of a protein. Rather, Yu et al. teach *expression of the Gam gene within cells that also express RecBC nuclease* to allow genetic integration of linear DNA fragments to occur within the same cells. In asserting that Yu et al. provide motivation for the claimed invention, the Office Action further states on page 5 that ". . . the use of a protein inhibitor of recB as taught by Yu et al. would be substantially simpler than

the method of Gold and Schweiger et al., requiring merely the addition of a protein to the ITT extract . . . a skilled artisan would clearly have been motivated to use the approach taught by Yu et al." Applicants dispute that Yu et al. teach the use of a protein inhibitor that requires "merely the addition of a protein" to the ITT extract. Yu et al. teach expression of a protein (Gam) within a live cell that is engineered to contain and express the Gam gene, and, further, the cell that is engineered by Yu et al. to express the Gam gene also produces the enzyme (recBC) that is to be inhibited by the in vivo synthesized protein (Gam). Thus, Yu et al. do not disclose an extract, do not teach addition of anything to any extract, and certainly do not teach the addition of a protein to an extract.

Third, one of ordinary skill in the art, in adding Gam protein to an E. coli extract to produce an in vitro synthesis system, would not have a reasonable expectation of success in producing an in vitro synthesis system. At the time the invention was made, it was not known whether addition of Gam protein to an E. coli cell extract would protect linear DNA molecules from degradation, or if the use of Gam protein in an in vitro synthesis system would adequately reduce or eliminate recBC activity, or whether it would interfere with transcription and/or translation. Applicants have demonstrated in the specification, however, that the addition of Gam protein to an E. coli extract does protect a linear DNA from degradation (Example 6) and that addition of Gam protein to an in vitro synthesis system is not detrimental to protein synthesis from linear or supercoiled DNA templates, and leads to enhanced production of protein in systems having a linear DNA template (Example 7).

The present invention includes a cell extract modified by the addition of Gam protein, a feature of the invention not taught or suggested by the references, in which the protein can reduce unwanted activity of an enzyme (recBC) at the appropriate time and in a titratable manner. Furthermore, no reasonable expectation of success was present at the time the invention was made, that in vitro protein or nucleic acid synthesis would occur in an extract that included added Gam protein. Thus, Applicants assert that a prima facie case for obviousness has not been established. Applicants therefore respectfully request that the rejection under 35 U.S.C. §103(a) of claims 1, 41, and 51, and of claims 16, 17, 28, 30, 55, 61, 62, 85-87, and 94-96 that depend from claim 1, of claims 57, 69, 70, and 91-93 that depend from claim 41; and of claims 52-54,

60, 77, 78, and 94 that depend from claim 51, be removed. The rejection of claims 39, 56, and 88 is rendered moot by their cancellation herein.

Claims Rejections under 35 U.S.C. §103(b), Pratt, Yu et al., and Swartz et al.

Claims 86, 87, 92, 93, 95, and 96 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Pratt in view of Yu et al. and further in view of Swartz et al. (WO 00/55353). Applicants respectfully traverse this rejection. Claims 86 and 87 depend from claim 1, claims 92 and 93 depend from claim 41, and claims 95 and 96 depend from claim 51. For the reasons set forth above, Applicants assert that claims 1, 41, and 51 are nonobvious with respect to Pratt and Yu et al. Applicants assert that Swartz does not make up for the deficiencies of Pratt and Yu et al., in that Swartz also does not disclose or suggest Gam protein or the addition of Gam protein to an E. coli lysate. Thus, not all elements of claims 86, 87, 92, 93, 95, and 96 are presented in the cited references, and a prima facie case for obviousness under 35 U.S.C. §103(a) is not made. The claims are therefore patentable under 35 U.S.C. §103(a) and Applicants respectfully request that the rejection be removed.

Claims Rejections under 35 U.S.C. §103(b), Pratt, Yu et al., and Swartz et al.

Claims 61, 62, 69, 70, 77, and 78 have been rejected under as being unpatentable under 35 U.S.C. §103(a) over Pratt in view of Yu et al. and further in view of Kudlicki et al. (U.S. Patent 6,664,379). Applicants respectfully traverse this rejection. Claims 61 and 62 depend from claim 1, claims 69 and 70 depend from claim 41, and claims 77 and 78 depend from claim 51. Applicants assert that no prima facie case for rejection under has been made, in that suggestion, motivation, and a reasonable expectation of success in adding Gam to an E. coli lysate are not present, and that in not all of the claims elements of the claimed in vitro synthesis system are present in Pratt and Yu, as provided in the arguments above. In particular, neither Pratt nor Yu et al. disclose Gam protein. Kudlicki does not make up for the deficiencies of Pratt and Yu et al., in that Kudlicki does not disclose Gam protein. Thus, not all elements of claims 86, 87, 92, 93, 95, and 96 are presented in the cited references, and a prima facie case is not made. The claims are

therefore patentable under 35 U.S.C. §103(a) and Applicants therefore respectfully request that the rejection be removed.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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